PATENT
Our Docket: P-LA 1245

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Border and Ruoslahti	Group Art Unit: 1644
Serial No: 08/349,479	Examiner: P. Gambel
Filed: December 2, 1994	
For: INHIBITING TRANSFORMING GROWTH FACTOR β TO PREVENT ACCUMULATION OF EXTRACELLULAR MATRIX	

Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

I, Lucia L. Languino, hereby declare as follows:

1. I am currently an Associate Professor of Pathology at Yale University School of Medicine. I have been a faculty member at Yale University School of Medicine since 1994.

2. I received a doctorate in Pharmacology from the Negri Institute of Pharmacological Research, Milan, Italy in 1984. I was a post-doctoral fellow in the laboratory of Erkki Ruoslahti, M.D., Ph.D., at The Burnham Institute, known at that time as the La Jolla Cancer Research Foundation, from 1987 to 1991.

3. I understand that the claims pending in the above-identified application stand rejected, in part, based on the assertion that the Applicants have allegedly not shown conception prior to December 22, 1988, of the use of anti-TGF-β antibodies to decrease the deleterious TGF-β-induced production and accumulation of extracellular matrix (ECM) associated with a pathology or condition.

4. I was a postdoctoral fellow in Dr. Ruoslahti's laboratory during the time period Dr. Border conducted research related to the above-identified patent application in Dr. Ruoslahti's laboratory. Prior to December 22, 1988, I was asked by Drs. Border and Ruoslahti to assist in the preparation of anti-TGF-β antibodies against amino acids 78 to 109 of TGF-β for a stated goal of using anti-TGF-β antibodies to inhibit TGF-β in order to decrease the deleterious TGF-β-induced production and accumulation of extracellular matrix (ECM) associated with a disease, including kidney disease.

5. As evidence of my communications, prior to December 22, 1988, with Drs. Border and Ruoslahti, attached to this Declaration as Exhibit A, is a La Jolla Cancer Research Foundation animal usage form related to the project entitled "Anti-human TGF-β Cyclized Peptide," which lists Dr. Border and myself as the investigators. The date of Exhibit A, which is prior to December 22, 1988, has been redacted. The animal usage form was submitted for the goal of generating an inhibitory antibody that would inhibit TGF-β binding to cells and, therefore, inhibit TGF-β activities, including ECM production.

6. Therefore, I can corroborate, based on personal observations and communications as described in the foregoing paragraphs, that Drs. Border and Ruoslahti prior to December 22, 1988, conceived of using anti-TGF-β antibodies to inhibit TGF-β in order to decrease the deleterious TGF-β-induced production and accumulation of extracellular matrix (ECM) associated with a disease, including kidney disease.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

3/12/01
Date

Lucia R. Languino

LA JOLLA CANCER RESEAR FOUNDATION

ANIMAL USAGE FORM

AUF 1413

PLEASE TYPE OR PRINT

1. PRINCIPAL INVESTIGATOR: WAYNE A. BORDER, M.D. | OFFICE PHONE: 226 | HOME/EMERGENCY PHONE: (714) 770-4602

2. OTHER INVESTIGATOR: LUCIA LANGUINO, Ph.D. | 230 | 539-0609

3. SENIOR TECHNICIAN:

4. PROJECT TITLE: ANTI-HUMAN TGFβ CYCLIZED PEPTIDE

5. GRANT NUMBER, IF ANY: 250200 | NEW: X | RENEWAL: | PILOT: | PROJECT NUMBER:

6. START DATE: | END DATE: | QUANTITY: MICE: | RATS: | RABBITS: 2 | GPs: | OTHER (SPECIFY):

7. PROJECT GOAL (SEE INSTRUCTIONS)

To produce quantities of anti-human TGFβ cyclized peptide for use in kidney disease research.

8. RATIONALE (SEE INSTRUCTIONS)

Rabbits produce high quality antiserum which can be used for identification of human TGFβ in tissue samples and in vitro assays to study progression of kidney injury.

9. DESCRIBE USE OF ANIMALS (SEE INSTRUCTIONS)

All injections/bleedings to be performed by animal care facility personnel.

1. Pre-bleeding 20 ml from ear vein .
2. Inject 500 μg TGFβ cyclized purified peptide (0.5 ml antigen in PBS + 0.5 ml FCA) subcutaneously in 2 sites.
3. After one month, boost with 125 μg antigen (0.25 ml antigen in PBS + 0.25 ml incomple adjuvant) subcutaneously, 2 sites.
4. After 10 days, bleed 50 ml from alternating ear veins 3 times.
5. Repeat steps 3-4 at 4-6 week intervals.

[illegible] RESEARCH PROTOCOL

10. PAIN LEVEL - A [X] B [ ] C [ ] (IF B OR C READ INSTRUCTIONS. PROVIDE DESCRIPTION OR JUSTIFICATION HERE)

CONFIDENTIAL

11. EUTHANASIA (SEE INSTRUCTIONS)

DURING PROJECT [ ] | END OF PROJECT [X] | METHOD OR TECHNIQUE | CO2 [ ] | I.V. [X] | CERV. DISLOC. [ ] | OTHER (SPECIFY) | RETAIN CARCASSES FOR PI: YES [ ] NO [X]

12. SIGNATURES

PI: WA Border DATE

U2 05334 DATE

AP MGR DATE

FORM AP 288 REV 1/96

DISTRIBUTION: WHITE TO FILE CANARY TO PI PINK - EXTR.